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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,657	10/24/2003	Sylvain Chemtob	50429/005001	1182

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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
HISSONG, BRUCE D	
ART UNIT	**PAPER NUMBER**
1646	

MAIL DATE	DELIVERY MODE
04/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/693,657	CHEMTOB ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *1-11,14-17,19-22,24-26 and 28-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12,13,18,23 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/19/04, 2/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence comparison 1 and 2*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Invention 9, claims 12, 13, 18, 23 and 27 in the reply filed on 4/20/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Applicant's election with traverse of VEGFR residues 320-350, which is SEQ ID NO: 2, in the reply filed on 4/20/2006 is acknowledged. The traversal is on the ground(s) that there would be no undue burden to search the residues recited in claim 13 because the claimed residues are all derived from the VEGFR sequence, and the claimed residues share structural and functional similarities. Furthermore, the Applicants argue that the claimed regions were presented in proper Markush format, and because the claimed residues with said Markush group share a common utility and substantial structural features essential to that utility, the claimed residues should be examined together.

These arguments have been fully considered and are not found persuasive. The claimed VEGFR residues are non-overlapping peptides, and are thus different regarding both sequence and overall structure. Searching all non-overlapping sequences would constitute a serious search burden.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-37 are currently pending. Claims 1-11, 14-17, 19-22, 24-26, and 28-37 are withdrawn as non-elected subject matter, and claims 12, 13, 18, 23, and 27 are the subject of this office action.

Information Disclosure Statement

1. The information disclosure statement received on 11/19/2004 has been fully considered by the Examiner.

2. The information disclosure statement received on 2/28/2005 has been considered by the Examiner. References C1-C22 have been lined-through because they were cited in the information disclosure statement received on 11/19/2004. References A1 and B1 have been considered.

3. The information disclosure statement received on 3/4/2005 has not been considered because all cited references were submitted in the information disclosure statement received on 11/19/2004.

Specification

The specification contains sequence listings that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, the instant application fails to comply with the requirements of 37 CFR 1.821 – 1.825. Specifically, the sequences disclosed in Figures 3-7 and 11-13 are not accompanied by the required sequence identifiers. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 – 1.825), and identify all sequences by sequence identifier.

Claim Objections

1. The Examiner suggests amending claim 12 to recite "a peptide comprising from about 7 to about 20 amino acids.....".

2. Claims 13, 23, and 27 are objected to for reciting non-elected subject matter. Due to the election of VEGFR residues 320-350, and SEQ ID NO: 2, the recitation of other residues or SEQ ID NOs is a recitation of non-elected subject matter.

Claim Rejections - 35 USC § 112, first paragraph – enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12, 13, 18, 23, and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the cytokine receptor peptide antagonists described in the examples of the specification, does not reasonably provide enablement for any other peptide antagonist "derived from" a cytokine receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to non-competitive extracellular cytokine receptor antagonists, wherein said antagonists are peptides "derived" from a flexible region of a cytokine receptor, or in the case of claim 27, are peptidomimetics of a peptide antagonist. The specification provides guidance and examples showing various peptide antagonists for VEGFR, IGF-1R, IL-4R, and IL-1R (see Examples 1-4), and discloses examples of peptides that function to inhibit activity mediated via these cytokine receptors. However, the specification defines peptides "derived from a flexible region" as peptides of 5 to about 20 amino acids that have been generated to correspond to segments of 5 to 20 contiguous amino acids located anywhere in the flexible regions, and that may have been subjected to further modification or "functional derivation" (see paragraph 0031). Furthermore, a "flexible region of a receptor" can refer to any region of a receptor that possesses sufficient flexibility to bend, extent, twist, or otherwise change it's conformation, and includes regions such as α helix, β sheet, loops, β turns, and flexible regions between domains of the receptor (see paragraph 0023). Thus, when interpreted in light of the specification, the breadth of the claims is excessive because they read on peptide antagonists "derived" by any "functional derivation" from a large number of potential residues or regions of a receptor. The specification does not provide sufficient guidance or examples that would show a person of ordinary skill in the art how to "derive" a peptide having any type of "functional derivation". Given the broadest reasonable interpretation, the claimed peptides could be interpreted as being derived from a sequence identical to a region in a receptor, or possess reversed sequence/chirality as described in the specification. However, the specification does not limit the "derived" peptides to these types of modifications, and thus the nature of the "functional derivation" could be almost anything. Claim 27 is also drawn to a peptidomimetic of a peptide "derived" from a cytokine receptor. Although the specification provides general guidance on how such peptidomimetics could be made, there are no examples of any peptidomimetics that function as cytokine receptor antagonists, or any specific guidance and examples as to regions of secondary structure necessary for recognition and activity towards a

cytokine receptor, or how to use "conformationally constrained dipeptide surrogates" to "refine backbone geometry" of the claimed peptidomimetics.

It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. As an example of the unpredictable effects of mutations on protein function, Mickle *et al* (Med. Clin. North Am., 2000, Vol. 84(3), p. 597-607) teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR – p. 597). Several mutations can cause cystic fibrosis, including the G551D mutation. In this mutation, a glycine replaces the aspartic acid at position 551, giving rise to the cystic fibrosis phenotype. In the most common cystic fibrosis mutation, Δ-F508, a single phenylalanine is deleted at position 508, giving rise to the cystic fibrosis phenotype. Thus, even the substitution or deletion of a single amino acid can have dramatic and *unpredictable* effects on the function of the protein.

Given this unpredictability inherent in the art regarding unlimited modifications or changes to a protein or peptide primary amino acid sequence, a person of ordinary skill in the art would not be able to predict which of the many possible modifications or derivations could result in a peptide that is an effective inhibitor of a cytokine receptor, wherein said peptide is "derived" from any "flexible region" of a cytokine receptor, or is any peptidomimetic of any peptide derived from any flexible region of a cytokine receptor. Therefore, a person of ordinary skill in the art would require further, undue experimentation in order to make and use any peptide antagonists of cytokine receptors other than those disclosed in Examples 1-4, without further, undue experimentation.

Finally, the claims are also broad in that claim 13 recites a cytokine receptor antagonist, wherein the cytokine receptor is human VEGFR, and said antagonist is a peptide derived from a VEGFR region. The claim does not specify that the peptide is also derived from human VEGFR, and thus reads on peptides derived from all possible VEGFR polypeptides. There is no guidance or examples in the specification showing how to make and use a human VEGFR antagonist peptide "derived from" VEGFR polypeptides of any other species. Furthermore, the claim reads on a peptide derived form amino acids 320-350 of VEGFR. The specification does not teach that amino acids 320-350 are the same in all possible VEGFR sequences, and because there is no specific sequence for VEGFR recited in the claims, a skilled artisan would not know how to make and use a peptide derived from amino acids 320-350 of all possible

VEGFR sequences. Therefore, one of ordinary skill in the art, for the reasons discussed above relating to unpredictable effects of polypeptide mutations, would not be able to predict how to make and use a human VEGFR peptide antagonist derived from any polypeptide that is not identical to human VEGFR.

Claim Rejections - 35 USC § 112, first paragraph – written description

Claims 12, 13, 18, 23, and 27 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite a peptide that is "derived from" a flexible region of a cytokine receptor. As set forth *supra* in the rejection under 35 U.S.C. 112, first paragraph, enablement, a peptide that is "derived from" a flexible region of any cytokine receptor can comprise a peptide having any type of "functional derivation", and can originate from a large number of potential regions on said cytokine receptor. The instant specification does not describe all possible functional derivations from all possible flexible regions of all possible cytokine receptors, including the nature or location of such derivations. Thus, the claims are drawn to a genus of "derived" peptides that have not been adequately described in the specification. Furthermore, as discussed *supra*, the claims are also drawn to a genus of human VEGFR antagonists derived from all possible VEGFR polypeptides, including non-human VEGFR polypeptides, and specifically peptides derived from amino acids 320-350 of all possible VEGFR polypeptides. Because the claims do not identify human VEGFR by specific sequence identifier, the claims read on any and all possible VEGFR sequences, and this genus of sequences has also not been adequately described in the instant specification.

Claim 27 is also drawn to a antagonist that is a peptidomimetic of a peptide having a sequence set forth in SEQ ID NOs 1-3. The claim does not require the peptidomimetics of the instant invention to have any particular activity other than be a cytokine antagonist, nor particular structure or any disclosure of which peptide regions or residues that peptidomimetics must be derived from, or any disclosure of any specific peptidomimetics that function as cytokine receptor antagonists and which were in the Applicants' possession at the time the

instant invention was filed. Thus, the claim is drawn to a genus of peptidomimetics that has not been adequately described in the specification.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a requirement that the claimed antagonist be "derived from" a flexible region of any cytokine receptor, including all possible VEGFR sequences, or be a peptidomimetic of a peptide antagoinst. There is no identification of any particular portion of said peptide that must be conserved in order to maintain function. Accordingly, in the absence of sufficient distinguishing characteristics, the specification does not provide adequate written description of the claimed genus of peptides "derived from" a flexible region of a cytokine receptor, including all possible VEGFR sequences, or the claimed genus of peptidomimetics.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the peptides described in examples 1-4 of the instant specification, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first

paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 13, 18, 23, and 27 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 13 recites the acronym VEGFR. Acronyms should be defined upon the first use in a claim, and without a proper identification/definition, the claims are indefinite. Claim 13 further recites a cytokine receptor antagonist, wherein said cytokine receptor is human VEGF and said peptide is derived from various VEGFR regions. However, the VEGFR sequence is not identified by a sequence identifier, and therefore it is not clear which VEGFR sequence the claimed regions are derived from, or if the recited regions are also from human VEGFR or from any other VEGFR sequence.

2. Claims 18, 23, and 27 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn methods of inhibiting human VEGFR activity; however, the claims do not recite any specific activity, and therefore the metes and bounds of the term "activity" are not defined. For example, the term "activity" could be interpreted as a non-specific *in vitro* activity (e.g. as a substrate for a protease), or any *in vivo* activity, both non-specific and specific to VEGFR.

3. Claims 18, 23, and 27 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims are drawn to a method of inhibiting VEGFR activity comprising "targeting" VEGFR with an antagonist. As currently written, the metes and bounds of the term "targeting" are unclear. The omitted steps are a step that disclosed how VEGFR is

targeted or describes the nature of said "targeting", and a step that discloses an intended target cell or individual, and a conclusion step that demonstrates that VEGFR has been targeted.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 12 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Tan *et al* (cited in the information disclosure statement received on 11/19/2004). The claim is drawn to a non-competitive extracellular cytokine receptor antagonist, wherein said antagonist is a peptide containing from about 7 to about 20 amino acids. The claim further recites that the peptide antagonist is derived from a flexible region of a cytokine receptor.

Tan *et al* teaches a peptide inhibitor of VEGF comprising 11 amino acids (see abstract) that is capable of inhibiting VEGF activity (p. 151-154). Furthermore, because the metes and bounds of a peptide "derived from" a cytokine receptor are not clear (see 1st rejection under 35 U.S.C. 112, 2nd paragraph, above) the peptide antagonist of Tan *et al* can be considered, in the absence of evidence to the contrary, to be "derived from" a cytokine receptor. Because the USPTO does not have the facilities for testing the peptide antagonist of Tan *et al*, the burden is on the applicant to show a novel and unobvious difference between the claimed peptide antagonists and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). Furthermore, the claims are drawn to peptides that can be "derived from" a flexible region of a cytokine receptor. Thus, the peptide of Tan *et al* could be "derived from" the region of VEGRF amino acids 320-350 by replacing and/or deleting amino acids until the sequence disclosed by Tan *et al* is "derived", and therefore Tan *et al* also meets the limitations of claim 13.

2. Claims 12 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Binetruy-Tournaire *et al* (*EMBO J.*, 2000, Vol. 19, p. 1525-1533). The claim is drawn to a non-competitive extracellular cytokine receptor antagonist, wherein said antagonist is a peptide

containing from about 7 to about 20 amino acids. The claim further recites that the peptide antagonist is derived from a flexible region of a cytokine receptor.

Binetruy-Tournaire *et al* teaches a peptide inhibitor of VEGF comprising 7 amino acids (see abstract, Table 1). This peptide is capable of binding to VEGFR (p. 1528 and Fig. 4), and inhibits VEGF activity *in vitro* and *in vivo* (p. 1528-1529). Furthermore, because the metes and bounds of a peptide "derived from" a cytokine receptor are not clear (see 1st rejection under 35 U.S.C. 112, 2nd paragraph, above) the peptide antagonist of Binetruy-Tournaire *et al* can be considered, in the absence of evidence to the contrary, to be "derived from" a cytokine receptor. Because the USPTO does not have the facilities for testing the peptide antagonist of Binetruy-Tournaire *et al*, the burden is on the applicant to show a novel and unobvious difference between the claimed peptide antagonists and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). Furthermore, the claims are drawn to peptides that can be "derived from" a flexible region of a cytokine receptor. Thus, the peptide of Binetruy-Tournaire *et al* could be "derived from" the region of VEGRF amino acids 320-350 by replacing and/or deleting amino acids until the sequence disclosed by Binetruy-Tournaire *et al* is "derived", and therefore Binetruy-Tournaire *et al* also meets the limitations of claim 13.

3. Claims 12, 13, 18, 23, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomas *et al* (US 5,712,380). The claims of the instant invention are drawn to a non-competitive extracellular cytokine receptor antagonist, wherein said antagonist is a peptide containing from about 7 to about 20 amino acids, wherein said peptide antagonist is derived from a flexible region of a cytokine receptor. The claims are further drawn to a antagonist derived from residues 320-350 of VEGFR, methods of inhibiting VEGFR activity with said antagonists, and methods of inhibiting VEGRF activity with a peptide having a sequence from SEQ ID NO: 2, or a peptidomimetic thereof.

Thomas *et al* teaches inhibitors of VEGF, and specifically teaches a peptide having a sequence in common with amino acids 320-250 of VEGFR, and specifically, with SEQ ID NO: 2 (see sequence comparison 1). Thomas *et al* also teaches methods of inhibiting VEGF activity by administration of VEGF peptide inhibitors (see column 8, lines 57-67, and Examples 4-5). Because the language of claim 12 is open-ended, this sequence can be interpreted as a sequence "containing" (or comprising) from about 7 to about 20 amino acids. Furthermore, due

to the high degree of homology between this peptide sequence and that of SEQ ID NO: 2, the sequence of Thomas *et al* can also be interpreted as being "derived from" a flexible region of the VEGFR, and specifically from the region of amino acids 320-350 of VEGFR. It is also noted that claims 23 and 27 recite a peptide having a sequence from SEQ ID NO: 2. Although the sequence of Thomas *et al* is not 100% identical to SEQ ID NO: 2, it has a sequence in common with SEQ ID NO: 2. Therefore, by teaching an antagonist peptide containing/comprising from about 7 to about 20 amino acids derived from the VEGFR, and specifically from amino acids 320-350 of SEQ ID NO, and furthermore having a sequence of SEQ ID NO: 2, as well as methods of administering said peptide, Thomas *et al* meets the limitations of the claims of the instant invention. Furthermore, the sequence of Thomas *et al* could also be interpreted as a peptidomimetic that is "derived from" a VEGFR sequence, and therefore Thomas *et al* also meets the limitations of claim 27

4. Claims 12, 13, 18, 23, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Davis-Smyth *et al* (5,952,199). The claims of the instant invention are drawn to a non-competitive extracellular cytokine receptor antagonist, wherein said antagonist is a peptide containing from about 7 to about 20 amino acids, wherein said peptide antagonist is derived from a flexible region of a cytokine receptor. The claims are further drawn to a antagonist derived from residues 320-350 of VEGFR, methods of inhibiting VEGFR activity with said antagonists, and methods of inhibiting VEGRF activity with a peptide having a sequence from SEQ ID NO: 2, or a peptidomimetic thereof.

Davis-Smyth *et al* teaches inhibitors of VEGF, and specifically teaches a peptide having a sequence in common with amino acids 320-250 of VEGFR, and specifically, with SEQ ID NO: 2 (see sequence comparison 2). Davis-Smyth *et al* also teaches methods of inhibiting VEGF activity by administration of VEGF peptide inhibitors (see column 19, line 47 – column 21, line 23). Because the language of claim 12 is open-ended, this sequence can be interpreted as a sequence "containing" (or comprising) from about 7 to about 20 amino acids. Furthermore, due to the high degree of homology between this peptide sequence and that of SEQ ID NO: 2, the sequence of Davis-Smyth *et al* can also be interpreted as being "derived from" a flexible region of the VEGFR, and specifically from the region of amino acids 320-350 of VEGFR. It is also noted that claims 23 and 27 recite a peptide having a sequence from SEQ ID NO: 2. Although the sequence of Davis-Smyth *et al* is not 100% identical to SEQ ID NO: 2, it has a sequence in

common with SEQ ID NO: 2. Therefore, by teaching an antagonist peptide containing/comprising from about 7 to about 20 amino acids derived from the VEGFR, and specifically from amino acids 320-350 of SEQ ID NO, and furthermore having a sequence of SEQ ID NO: 2, as well as methods of administering said peptide, Davis-Smyth *et al* meets the limitations of the claims of the instant invention. Furthermore, the sequence of Davis-Smyth *et al* could also be interpreted as a peptidomimetic that is "derived from" a VEGFR sequence, and therefore Davis-Smyth *et al* also meets the limitations of claim 27

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
Art Unit 1646

ROBERT S. LANDSMAN, PH.D
PRIMARY EXAMINER

SEQUENCE COMPARISON 1

```
RESULT 1
US-08-232-538-13
; Sequence 13, Application US/08232538
; Patent No. 5712380
;  GENERAL INFORMATION:
;    APPLICANT:  Thomas, Kenneth A.
;    APPLICANT:  Kendall, Richard L.
;    TITLE OF INVENTION:  INHIBITOR OF VASCULAR ENDOTHELIAL CELL
;    TITLE OF INVENTION:  GROWTH FACTOR
;    NUMBER OF SEQUENCES:  18
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Merck & Co., Inc.
;      STREET:  P.O. Box 2000 126 E Lincoln Avenue
;      CITY:  Rahway
;      STATE:  NJ
;      COUNTRY:  USA
;      ZIP:  07065-0907
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/232,538
;      FILING DATE:
;      CLASSIFICATION:  514
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Wallen, John W.III
;      REGISTRATION NUMBER:  35,403
;      REFERENCE/DOCKET NUMBER:  18888IA
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (908) 594-3905
;      TELEFAX:  (908) 594-4720
;  INFORMATION FOR SEQ ID NO:  13:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  668 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
US-08-232-538-13

  Query Match             95.7%;  Score 45;  DB 1;  Length 668;
  Best Local Similarity   90.0%;  Pred. No. 0.96;
  Matches    9;  Conservative    1;  Mismatches    0;  Indels    0;
Gaps    0;

Qy          1 EATVGERVRL 10
              |||||||||:
Db        345 EATVGERVRI 354
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SEQUENCE COMPARISON # 2

```
RESULT 4
US-08-874-678-2
; Sequence 2, Application US/08874678
; Patent No. 5952199
;  GENERAL INFORMATION:
;    APPLICANT:  Davis-Smyth, Terri L.
;    APPLICANT:  Chen, Helen H.
;    APPLICANT:  Presta, Leonard
;    APPLICANT:  Ferrara, Napoleone
;    TITLE OF INVENTION:  NOVEL INHIBITORS OF VASCULAR ENDOTHELIAL GROWTH
FACTOR
;    TITLE OF INVENTION:  ACTIVITY, THEIR USES AND PROCESSES FOR THEIR
PRODUCTION
;    NUMBER OF SEQUENCES:  48
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Flehr, Hohbach, Test, Albritton & Herbert
;      STREET:  Four Embarcadero Center, Suite 3400
;      CITY:  San Francisco
;      STATE:  California
;      COUNTRY:  United States
;      ZIP:  94111-4187
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.30
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/874,678
;      FILING DATE:  HEREWITH
;      CLASSIFICATION:  435
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 08/643,839
;      FILING DATE:  07-MAY-1996
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Dreger, Walter H.
;      REGISTRATION NUMBER:  24,190
;      REFERENCE/DOCKET NUMBER:  A-63291-1/WHD
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (415) 781-1989
;      TELEFAX:  (415) 398-3249
;      TELEX:  910 277299
;  INFORMATION FOR SEQ ID NO:  2:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  767 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:  unknown
;      TOPOLOGY:  unknown
;    MOLECULE TYPE:  protein
US-08-874-678-2

  Query Match             95.7%;  Score 45;  DB 1;  Length 767;
  Best Local Similarity   90.0%;  Pred. No. 1.1;
  Matches    9;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EATVGERVRL 10
              |||||||||:
Db        341 EATVGERVRI 350
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